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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,753	09/14/2005	Roger Kenneth Smith	2985-1-001	6929

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EXAMINER	
BERTOGLIO, VALARIE E	

ART UNIT	PAPER NUMBER
1632	

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11/01/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/526,753	SMITH ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-16,20,22,23,35,36 and 38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-16,20,22,23,35,36 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's reply filed on 12/18/2009 is acknowledged. Claim 3,17-19,21,24-34,37,39 and 40 are cancelled.

Claims 1,2,4-16,20,22-23,35-36,38 are pending and are under consideration in the instant office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

The rejection of claims 1-16,20-23 and 34-40 under 35 U.S.C. 112, first paragraph, because the specification is not enabling for the full breadth of the claims is withdrawn in favor of the following rejection.

Claims 1,2,4-16,20,22-23,35-36,38 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of

the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The invention relates to use of cells isolated from bone marrow, expansion of said cells in culture, and introducing the expanded cells into a tendon injury of an injury to cause healing.

The claims have been amended to require use of cultured bone marrow cells in combination with bone marrow supernatant to cause soft skeletal tissue healing. Claims previously did not require healing and did not require culture of bone marrow cells. Claim 1 recites the alternative use of a composition enriched for mesenchymal stem cells (any composition, not necessarily the cultured bone marrow cells) and tenocytes in bone marrow supernatant to cause healing of soft skeletal tissue.

The following issues previously deemed non-enabled under scope of enablement stand as set forth below.

No breadth of the claims as currently amended is found enabled by the specification or art at the time of filing. Claims no longer encompass direct injection of bone marrow aspirate (which as previously taught in the art) and now require a treatment effect including regeneration of tissue by cultured cells. The claims are amended to now read that bone marrow cells are cultured to generate a composition enriched for MSCs.

The specification teaches the culture and expansion of a cell type that is referred to as MSCs wherein the cells are isolated from bone marrow aspirate. These cells are spun down and resuspended in plasma, which contains a plentiful supply of growth factors and platelets that are helpful in wound healing. The cells are not resuspended in bone marrow supernatant as claimed. The resulting suspension was used to treat, by direct, local injection, 6 horses with tendonopathy. Two appeared to recover quickly while the remaining subjects showed less change. These observations fail to demonstrate that the method promotes regeneration of the tissue as claimed. First, without comparison to an untreated control, one cannot determine that the regeneration observed was promoted by any administered composition and was not regeneration that would naturally occur. Second, the specification fails to teach any treatment by the

injected materials. The healing that is observed in Examples 1/2 could be the result of the injected stem cells, the injected plasma, or healing that naturally occurs absent the injected materials. As well, treatment using plasma fails to equate to treatment using the claimed bone marrow supernatant. Sutter (2007, Clinical Techniques in Equine Practice, 2007, 6:198-208) taught that platelet-rich plasma has high therapeutic value in promoting healing of an array of bodily injuries, including tendonitis (see page 200). Therefore, if the healing reported in the specification was the result of the treatment, the effect may have been caused by the plasma, not the cells and not the claimed bone marrow supernatant.

Finally, the specification teaches only the regeneration in tendonopathy, and does not teach regeneration of any soft skeletal tissue as claimed. Implanted MSCs will differentiate dependent upon the growth factors supplied. The specification fails to discuss the types of tissue formed by the stem cells, if any are formed at all. Therefore, the specification, while failing to teach that the claimed composition can treat tendonitis as set forth above, also clearly fails to teach regeneration of any soft skeletal tissue as is now recited in the claims.

There are several working examples using bone marrow aspirate directly, which includes bone marrow cells and bone marrow supernatant. However, the bone marrow cells in these examples are not cultured and therefore the cellular component of the composition used in these later examples are different from that claimed and thus, do not correlate to the claimed invention.

Additionally, the claims recite that, alternatively, a composition enriched for MSCs and tenocytes derived therefrom in bone marrow supernatant can be used. The claim, as written, fails to require that these MSCs come from bone marrow and therefore, encompass any MSC. However, because the composition administered in the working examples is not characterized and the presence of MSCs is not verified and, as well, other cellular components are not known, it is not clear that MSCs derived from any source would be capable of carrying out the required treatment.

The previous rejection of claim 17 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is rendered moot by the cancellation of the claim.

Written Description

The rejection of claims 1-17,20-23 and 34-40 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 1-17,20-23 and 34-40 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in light of Applicant's amendments to the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (c) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejection of claims 1-9,12-14,16,22 under 35 U.S.C. 102(b) as being anticipated by Herthel (Nov 2001, IDS) is withdrawn. Herthel did not teach in vitro culture as required by the claims.

The rejection of claims 1-6,12-14,22, 34-36 under 35 U.S.C. 102(b) as being anticipated by Awad (1999, IDS) is withdrawn. Awad did not teach use of bone marrow supernatant in combination with cultured MSCs.

The rejection of claims 1-6,12-15,21,23,34-36,39 and 40 under 35 U.S.C. 102(b) as being anticipated by US Patent No. 5,811,094 is withdrawn. '094 did not teach use of bone marrow supernatant.

The rejection of claims 1-7,12-14,16,21-23,34-36,39 and 40 under 35 U.S.C. 102(e) as being anticipated by US Patent No. 6,835,377 (filed 05/13/1998). '377 did not teach use of bone marrow supernatant in combination with cultured MSCs.

The rejection of claims 34, 37 and 38 under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,811,094 in view of Herthel (Nov 2001, IDS) is withdrawn.

The rejection of claims 34, 37 and 38 under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,835,377 (filed 05/13/1998) in view of Herthel (Nov 2001, IDS) is withdrawn.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is (571) 272-0725. The examiner can normally be reached on Mon-Thurs 5:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Valarie Bertoglio/
Primary Examiner, Art Unit 1632